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Dated: November 25, 2003 Signature:

(Mary Usene DiPalma)

Docket No.: HUIP-P04-009  
(PATENT)

## IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of:  
Melton et al.

Application No.: Not Yet Assigned

Confirmation No.: Not Yet Assigned

Filed: November 25, 2003

Art Unit: Not Yet Assigned

For: METHOD OF INDUCING AND  
MAINTAINING NEURONAL CELLS

Examiner: Not Yet Assigned

### INFORMATION DISCLOSURE STATEMENT (IDS)

MS Patent Application  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Dear Sir:

Pursuant to 37 CFR 1.56, 1.97 and 1.98, the attention of the Patent and Trademark Office is hereby directed to the references listed on the attached PTO/SB/08. It is respectfully requested that the information be expressly considered during the prosecution of this application, and that the references be made of record therein and appear among the "References Cited" on any patent to issue therefrom.

This Information Disclosure Statement accompanies the new patent application submitted herewith.

Those patent(s) or publication(s) listed in the attached form PTO/SB/08 are not supplied because they were previously cited by or submitted to the Office in a prior application number 08/835,279, filed April 9, 1997 and application number 08/403,007, filed March 9, 1995 and are relied upon in this application for an earlier filing date under 35 U.S.C. 120.

In accordance with 37 CFR 1.97(g), the filing of this Information Disclosure Statement shall not be construed to mean that a search has been made or that no other material information as defined in 37 CFR 1.56(a) exists. In accordance with 37 CFR 1.97(h), the filing of this

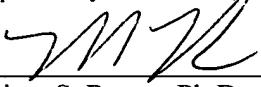
as defined in 37 CFR 1.56(a) exists. In accordance with 37 CFR 1.97(h), the filing of this Information Disclosure statement shall not be construed to be an admission that any patent, publication or other information referred to therein is "prior art" for this invention unless specifically designated as such.

It is submitted that the Information Disclosure Statement is in compliance with 37 CFR 1.98 and the Examiner is respectfully requested to consider the listed references.

The Director is hereby authorized to charge any deficiency in the fees filed, asserted to be filed or which should have been filed herewith (or with any paper hereafter filed in this application by this firm) to our Deposit Account No. 18-1945, under Order No. HUIP-P04-009. A duplicate copy of this paper is enclosed.

Dated: November 25, 2003

Respectfully submitted,

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Substitute for form 1449A/B/PTO  <b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  (Use as many sheets as necessary)				<b>Complete if Known</b>	
Sheet	1	of	3	Application Number	Not Yet Assigned
				Filing Date	November 25, 2003
				First Named Inventor	Douglas A. Melton
				Art Unit	N/A
				Examiner Name	Not Yet Assigned
				Attorney Docket Number	HUIP-P04-009

U.S. PATENT DOCUMENTS						
Examiner Initials*	Cite No. <sup>1</sup>	Document Number Number-Kind Code <sup>2</sup> (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	
AA		US-5,182,375	01-26-1993	Ling et al.		
AB		US-5,041,538	08-20-1991	Ling et al.		
AC		US-5,166,065	11-24-1992	Williams et al.		

FOREIGN PATENT DOCUMENTS						
Examiner Initials*	Cite No. <sup>1</sup>	Foreign Patent Document Country Code <sup>3</sup> -Number <sup>4</sup> -Kind Code <sup>5</sup> (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T <sup>6</sup>
BA		WO-89/01945	03/1989			

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. <sup>1</sup>Applicant's unique citation designation number (optional). <sup>2</sup> See Kinds Codes of USPTO Patent Documents at [www.uspto.gov](http://www.uspto.gov) or MPEP 901.04. <sup>3</sup>Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). <sup>4</sup>For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. <sup>5</sup>Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. <sup>6</sup>Applicant is to place a check mark here if English language Translation is attached.

NON PATENT LITERATURE DOCUMENTS						
Examiner Initials	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.				T <sup>2</sup>
CA		Mather, "Follistatin Modulates Activin Activity in a Cell-and Tissue-specific Manner," <i>Endocrinology</i> 132:2732-2734 (1993)				
CB		Attisano et al., "Novel Activin Receptors: Distinct Genes and Alternative mRNA Splicing Generate a Repertoire of Serine/Threonine Kinase Receptors," <i>Cell</i> 66:97-108 (1992)				
CC		Dohrmann et al., "Expression of Activin mRNA during Early Development in <i>Xenopus laevis</i> ," <i>Developmental Biology</i> 157:474-483 (1993)				
CD		Esch et al., "Structural Characterization of Follistatin: A Novel Follicle-Stimulating Hormone Release-Inhibiting Polypeptide from the Gonad," <i>Molecular Endocrinology</i> 1:849-855 (1987)				
CE		Green et al., "Responses of Embryonic <i>Xenopus</i> Cells to Activin and FGF Are Separated by Multiple Dose Thresholds and Correspond to Distinct Axes of the Mesoderm," <i>Cell</i> 71:731-739 (1992)				
CF		Hemmati-Bivanlou et al., "A Truncated Activin Receptor Inhibits Mesoderm Induction and Formation of Axial Structures in <i>Xenopus</i> Embryos," <i>Nature</i> 359:609-614 (1992)				
CG		Hillier et al., "Inhibin, Activin, and Follistatin Potential Roles in Ovarian Physiology," <i>Annals New York Academy of Sciences</i> 687:29-38 (1993)				
CH		Klar et al., "F-Spondin: A Gene Expressed at High Levels in the Floor Plate Encodes a Secreted Protein That Promotes Neural Cell Adhesion and Neurite Extension," <i>Cell</i> 69:95-110 (1992)				
CI		Kreidberg et al., "WT-1 Is Required for Early Kidney Development," <i>Cell</i> 74:679-691 (1993)				
CJ		Melton, "Pattern Formation During Animal Development," <i>Science</i> 252:234-241 (1991)				
CK		Paralkar et al., "Recombinant Human Bone Morphogenetic Protein 2B Stimulates PC12 Cell Differentiation: Potentiation and Binding to Type IV Collagen," <i>Journal of Cell Biology</i> 119:1721-1728 (1992)				
CL		Patthy et al., Functions of Agrin and Agrin-related Proteins, <i>TINS</i> 16(2):76-81 (1993)				
CM		Rosenberg et al., "Grafting Genetically Modified Cells to the Damaged Brain: Restorative Effects of NGF Expression," <i>Science (Reports)</i> 242:1575-1577 (1988)				

Examiner Signature		Date Considered	
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Substitute for form 1449A/B/PTO	Application Number	Not Yet Assigned			
	Filing Date	November 25, 2003			
	First Named Inventor	Douglas A. Melton			
	Art Unit	N/A			
	Examiner Name	Not Yet Assigned			
Sheet	2	of	3	Attorney Docket Number	HUIP-P04-009

CN	Schubert et al., "Activin is a Nerve Cell Survival Molecule," Nature 344:868-870 (1990)
CO	Sokol et al., "Interaction of Wnt and Activin in Dorsal Mesoderm Induction in Xenopus," Developmental Biology 154:348-355 (1992)
CP	Thomsen et al., "Processed Vg1 Protein is an Axial Mesoderm Inducer in Xenopus," Cell 74:433-441 (1993)
CQ	Buse et al., "Differentiation of the Mammalian Retinal Pigment Epithelium in vitro: Influence of Presumptive Retinal Neuroepithelium and Head Mesenchyme," Anatomy and Embryology 187:259-268 (1993)
CR	Gage et al., "Intracerebral Grafting: A Tool for the Neurobiologist," Neuron 6:1-12 (1991)
CS	Gurdon, "The Generation of Diversity and Pattern in Animal Development," Cell 68:185-199 (1992)
CT	Guthrie, "Horizontal and Vertical Pathways in Neural Induction," TINS 14:123-126 (1991)
CU	Langille et al., "Developmental Processes, Developmental Sequences and Early Vertebrate Phylogeny," Biology Review 64:73-91 (1989)
CV	Lemaire, "No Muscles, But What a Brain," Nature 359:586-587 (1992)
CW	McConnell, "The Generation of Neuronal Diversity in the Central Nervous System," Annual Review of Neuroscience 14:269-300 (1991)
CX	McKay, "The Origins of Cellular Diversity in the Mammalian Central Nervous System," Cell 58:815-821 (1989)
CY	Noden, "Spatial Integration Among Cells Forming the Cranial Peripheral Nervous System," Journal of Neurobiology 24:248-261 (1993)
CZ	Placzek et al., "Mesodermal Control of Neural Cell Identity: Floor Plate Induction by the Notochord," Science (Reports) 250:985-988 (1990)
CA1	Saint-Jeannet et al., "Experimentally Provoked Neural Induction Results in an Incomplete Expression of Neuronal Traits," Experimental Cell Research 207:383-387 (1993)
CB1	Smith et al., "Expression Cloning of Noggin, a New Dorsalizing Factor Localized to the Spemann Organizer in Xenopus Embryos," Cell 70:829-840 (1992)
CC1	Snyder et al., "Moltipotent Neural Cell Lines Can Engraft and Participate in Development of Mouse Cerebellum," Cell 68:33-51 (1992)
CD1	Stemple et al., "Isolation of a Stem Cell for Neurons and Glia from the Mammalian Neural Crest," Cell 71:973-985 (1992)
CE1	Tannahill et al., "Localized Synthesis of the Vg1 Protein During Early Xenopus Development," Development 106:775-785 (1989)
CF1	Wolswijk et al., "Identification of an Adult-specific Glial Progenitor Cell," Development 105:387-400 (1989)
CG1	Hashimoto et al., "Follistatin is a Developmentally Regulated Cytokine in Neural Differentiation," The Journal of Biol. Chem. 267(11):7203-7206 (1992)
CH1	Hashimoto et al., Activin/EDF as an Inhibitor of Neural Differentiation," Biochem. and Biophys. Research Comm. 173(1):193-200 (1990)
CI1	Hemmati-Brivanlou et al., "Inhibition of Activin Receptor Signaling Promotes Neuralization in Xenopus," Cell 77:273-281 (1994)
CJ1	Hemmati-Brivanlou et al., "Follistatin, an Antagonist of Activin, is Expressed in the Spemann Organizer and Displays Direct Neuralizing Activity," Cell 77:283-295 (1994)
CK1	Fukui et al., "Isolation and Characterization of Xenopus Follistatin and Activins," Developmental Biology 159:131-139 (1993)
CL1	Yamada et al., "Induction of Differentiation of the Human Promyelocytic Cell Line HL-60 by Activin/EDF," Biochem. Biophys. Res. Comm 187(1):79-85 (1992)
CM1	Reilly et al., "Short-Range Signaling by Candidate Morphogens of the TGFbeta Family and Evidence for a Relay Mechanism of Induction," Cell 86:743-754 (1996)
CN1	Asashima et al., "Role of Activin and Other Peptide Growth Factors in Body Patterning in the Early Amphibian Embryo," Int. Rev. Cytology 191:1-52 (1999)

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				Art Unit	N/A
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Sheet	3	of	3	Attorney Docket Number	HUIP-P04-009

	CO1	Chang et al., "Xenopus Type I Activin Receptor Mediates Mesodermal but not Neural Specification during Embryogenesis," Development 124:827-837 (1997)	
	CP1	Schuldiner et al., "Effects to Eight Growth Factors on the Differentiation of Cells Derived from Human Embryonic Stem Cells," PNAS 97(21):11307-11312 (2000)	

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<sup>1</sup>Applicant's unique citation designation number (optional). <sup>2</sup>Applicant is to place a check mark here if English language Translation is attached.

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